PATENT SPECIFICATION

800,973

Date of Application and filing Complete Specification June 20, 1955.

No. 17742/55.

Application made In United States of America on Aug. 13, 1954.

Complete Specification Published Sept. 3, 1958.

Index at acceptance: —Class 81(1), B3.

International Classification: —A61k.

COMPLETE SPECIFICATION

Improvements in or relating to Pills or Tablets

We, STERLING DRUG INC., a corporation organized and existing under the laws of the State of Delaware, United States of America, of 1450 Broadway, New York, State of New York, United States of America, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a multi-layered pill or tablet particularly adapted for medicinal use and having a medicinal core and an intervening taste-indicating alarm layer or lamination, said indicating lamination having an outer medicinal layer which is soluble in the patient's mouth, to the end that the pill is held by the patient for absorption of the outer layer until the taste-indicating layer is exposed, the taste-indicating layer serving as an indication to the patient to swallow the tablet to obtain the benefits of gastro-intestinal absorption of the medicament within the pill or tablet; and the provision of a pill or tablet as above described including a plurality of layers, so that different or succeeding spaced dosages may be administered, the core being covered by an enteric coating, and in the event that a plurality of layers of medicament are provided within the taste-indicating layer, such multiple layers may each be covered enterically.

Further objects of the invention include the provision of the alarm layer at the exterior of the tablet, so that when the alarm sensation ceases, the signal is thus given; the alarm material being mixed in with a medicament either at the exterior of the tablet or in an inner layer.

Other objects and advantages of the invention will appear hereinafter.

Reference is to be had to the accompanying drawings, in which:—

Fig. 1 is a cross section through a pill or tablet made according to the present invention; and

Fig. 2 is a modification thereof.

The present invention provides a means for dosing a patient with at least two separate medicaments, one of which is to be absorbed in the mouth and the other in the gastro-intestinal tract, with a definite period for the absorption of the orally applied medicament, so that the patient will not tend to hold the pill or tablet for too long or too short a time in the mouth and also providing a means for avoiding variation of the oral dosage due to lack of or more vigorous sucking on the tablet than might otherwise be the case.

To this end, the tablet is provided with an outer, medicinal coating 10 which is readily dissolved in the mouth, and directly under this layer there is a "signal" or "alarm" layer 12, so that the patient will know at once when the outer layer is gone and that the time has come to swallow the pill or tablet.

The "signal" or "alarm" layer 12 might be a taste-indicating layer, e.g., sodium chloride or quinine, or it might be of a substance which does not have a distinctive flavor but a different consistency from the outer layer 10, so that a signal is given the patient.

In other words, the tablet is intended to be retained by the patient in his mouth for absorption of the outer layer 10 which is a medicament, until the taste-indicating layer 12 is exposed. This serves as a signal for the patient to swallow the tablet.

Alternatively, the outermost layer may be the taste signal and oral medicament layer, which when gone, gives the signal to the patient to swallow the pill.

Reference numeral 14 indicates a medicament which will be dissolved in the gastro-intestinal tract after the taste-indicating layer is dissolved. Alternatively, there may be an enteric layer 16 intervening between the medicament 14 and taste-indicating layer 12 in order to provide a definite time of reception of the tablet in the stomach or other part of the body prior to release of the medicament 14. In this case, the layer 16 will be an enteric

layer as well known in the art, and may be of a thickness to release the contained medicine at a definite point in the travel of the pill through the gastro-intestinal tract.

The invention may of course be continued to provide other layers of medicament, enteric coatings, 18, and finally the core 20 of the final dosage to be given the patient.

The invention is further illustrated by the following examples without, however, being limited thereto:—

EXAMPLE 1

Tablets for the relief of asthma in which the prompt action of N—isopropylarterenol and the delayed action of theophyllin and benzylephedrine could be obtained were prepared as follows:—

A medicament core was prepared in the following manner: The following ingredients were weighed out separately, screened to 30 mesh, and mixed:—

Benzylephedrine	32.4	parts
Theophyllin	129.6	„
Phenobarbital	8.1	„
Starch	38.8	„
Talc	14.5	„
Stearic acid	2.3	„
Magnesium stearate	0.9	„

All parts by weight.

The mixture was slugged, screened to 12 mesh, and pressed on a $^{5}/_{16}$" concave tablet punch machine. The core was completed by applying three coats of shellac and talc.

An alarm mixture was prepared from the following ingredients:—

Citric acid	5	parts
Orange flavor	5	„
Sucrose	530	„

This mixture was applied as a dusting powder to the tablets moistened with 10% gelatin/30% sucrose aqueous syrup.

Then a mixture of N—isopropylarterenol (125 parts), sodium metabisulfite (30 parts), and talcum (125 parts) in 10% gelatin/30% sucrose aqueous syrup was applied to the tablets by tumbling.

Finally, the tablets were coated with 70% sucrose aqueous syrup until the tablets were smooth and well-covered, after which they were finished with a carnauba wax solution in conventional manner.

EXAMPLE 2

Tablets for the relief of angina by combining the prompt action of nitroglycerine with the more delayed action of pentaerithrytol tetranitrate were prepared in the following manner:—

The following ingredients were weighed up:—

Pentaerithrytol tetranitrate	2800	parts
Starch	500	„
Dicalcium phosphate	914	„
Alginic acid	86	„
Stearic acid	100	„

The ingredients were screened to 30 mesh, mixed, slugged, ground to 12 mesh, and pressed into tablets using a $^{13}/_{32}$" concave punch. The resulting tablets were given three coats of shellac, dusted with talc, and then an alarm layer was applied using an orange flavor in the same manner as in Example 1.

Thereafter the tablets were sugar-coated with 70% sucrose solution and then dusted after moistening with 10% gelatin until by assay the tablets contained a therapeutic dose of nitroglycerine. The nitroglycerine, being a detonation-sensitive liquid, is dusted safely as in the form of a 10% admixture on an inert solid diluent such as lactose. Thereafter the tablets were sugar-coated and polished with carnauba wax in conventional manner.

Instead of orange flavor and citric acid as the alarm component, other alarm components also used included mint, licorice and lemon flavors.

Instead of providing the alarm as a layer between the outer medicament layer and the core, the alarm may be mixed throughout the outer medicament layer, so that then the disappearance of the alarm sensation serves as a signal for the patient to swallow the tablet. This is shown in Fig. 2 wherein 22 indicates the core of medicament, 24 an interposed layer of medicament or coating, and 26 the outermost layer which is a medicated layer containing the alarm material in mixture therewith. In this case, the disappearance of the alarm sensation signals the patient to swallow the tablet, whereas if the alarm layer is interior, as at 12, the appearance is the signal. Also, of course, the interior signal layer 12 can be mixed with a medicament, and in this invention it is to be understood that the term "signal" or "alarm" layer may include medicament or not as circumstances call for.

WHAT WE CLAIM IS:—

1. A pill or tablet comprising an inner medicament layer or core, an outer mouth-soluble and absorbable medicament layer, and material in the pill providing a signal to the tongue when the outer medicament layer has been dissolved in the mouth.

2. A pill or tablet according to Claim 1, in which the signal material is provided in a separate layer between the medicament layers.

3. A pill or tablet according to Claim 2, in which the inner medicament layer or core is surrounded by an enteric coating.

4. A pill or tablet according to Claim 1, in which the signal material is incorporated in the outer medicament layer.

5. A pill or tablet according to any one of the preceding claims, in which the signal material is adapted to perform its function as a result of its taste being different from that of the adjacent layer.

6. A pill or tablet according to any one of Claims 1—4, in which the signal material is adapted to perform its function as a result of

its consistency being different from that of the adjacent layer.

7. The pills or tablets substantially as hereinbefore described with reference to and as illustrated in Figs. 1 and 2 of the accompanying drawings.

STEVENS, LANGNER, PARRY & ROLLINSON,
Chartered Patent Agents,
Agents for the Applicants.

Leamington Spa: Printed for Her Majesty's Stationery Office, by the Courier Press,—1958.
Published at the Patent Office, 25, Southampton Buildings, London, W.C.2, from which copies may be obtained.

800,973 COMPLETE SPECIFICATION
1 SHEET

This drawing is a reproduction of the Original on a reduced scale.

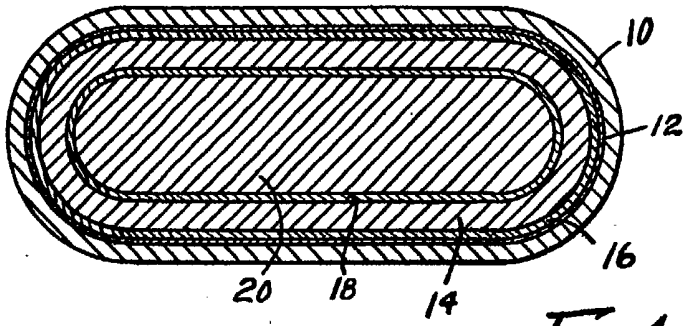

FIG. 1

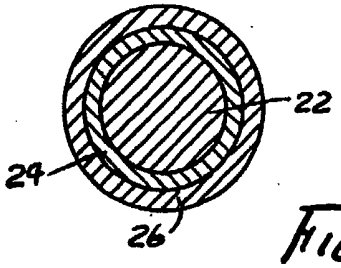

FIG. 2